



Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) Apparatus for detection of nucleotide hybridization comprising:
  - (a) cell walls defining a cell for holding a sample fluid;
  - (b) at least one working electrode mounted with an electrode surface in the cell, the electrode surface being configured for attachment to nucleotides;
  - (c) a counter-electrode mounted in the cell at a position spaced from the working electrode and positioned to be in contact with sample fluid in the cell;
  - (d) a high first frequency signal generator connected via a directional coupler to the working electrode to apply a signal at a high first frequency thereto;
  - (e) a low second frequency signal generator connected to the counter-electrode to provide a signal to the counter-electrode at a frequency lower than the high first frequency signal applied to the working electrode;
  - (f) a mixer connected via the directional coupler to the working electrode, the mixer adapted to receive a high-frequency signal reflected from the working electrode and connected to the high first frequency signal generator, the mixer providing an output signal that is the mix of the high first frequency signal from the high first frequency signal generator and the signal received through the directional coupler from the working electrode; and
  - (g) a signal detector adapted to receive ~~receiving~~ the output signal from the mixer and to detect ~~detecting~~ modulation of the high first frequency signal by the low second frequency signal thereby indicating hybridization.
2. (Currently amended) The apparatus of Claim 1 further including a reference electrode mounted in the cell spaced from the working electrode and the counter-electrode and positioned to be in contact with sample fluid in the cell, the low second frequency signal

generator connected to the counter-electrode through the positive input of a potentiostat having a negative input which is connected to the reference electrode.

3. (Currently amended) The apparatus of Claim 1 wherein the signal detector includes a lock-in amplifier receiving the output signal from the mixer and the signal from the ~~low~~ second frequency signal generator.

4. (Currently amended) The apparatus of Claim 1 wherein the ~~high~~ first frequency from the ~~high~~ first frequency signal generator is about 1 MHz and the ~~low~~ second frequency signal from the ~~low~~ second frequency signal generator is at about 1 kHz.

5. (Currently amended) The apparatus of Claim 1 further including a ~~high-pass filter~~ bias Tee connected between the directional coupler and the working electrode.

6. (Original) The apparatus of Claim 1 wherein there are a plurality of working electrodes mounted in the cell.

7. (Original) The apparatus of Claim 1 including an inlet channel extending to communication with the cell by which sample fluid may be provided to the cell, and an outlet channel extending from communication with the cell by which sample fluid may be discharged from the cell.

8. (Original) The apparatus of Claim 7 wherein the sample cell is formed in a multilayer structure having a base in which the working electrode is mounted and in which a conductor extending to the working electrode is embedded, an intermediate layer defining therein the inlet and outlet channels and peripheral walls of the cell, and a top layer having the counter-electrode embedded therein.

9. (Original) The apparatus of Claim 1 further comprising a self-assembled monolayer formed on the electrode surface of the working electrode.

10. (Withdrawn) A method of detecting hybridization of nucleotides bound to the surface of a working electrode comprising:

- (a) binding nucleotides to the surface of a working electrode within a sample cell;
- (b) applying a sample fluid into the sample cell, wherein the sample fluid may contain complements to the nucleotide bound to the working electrode;
- (c) applying a high frequency signal to the working electrode and a low frequency signal to a counter-electrode within the cell; and
- (d) detecting the signal reflected from the working electrode to determine the modulation of the high frequency signal by the low frequency signal which is thereby indicative of hybridization of the nucleotides in the sample fluid to the bound nucleotides.

11. (Withdrawn) The method of Claim 10 including forming a self-assembled monolayer on the surface of the working electrode before binding nucleotides thereto.

12. (Withdrawn) The method of Claim 10 wherein the high frequency signal is at about 1 MHz and the low frequency signal is about 1 kHz.

13. (Withdrawn) The method of Claim 10, wherein the working electrode comprised an electronic sensing region localized to up to 0.01 mm<sup>2</sup> in area.

14. (Currently amended) A system configured to detect nucleotide hybridization, the system comprising:

- (a) a fluid sample cell having at least one working electrode mounted therein and a counter electrode mounted therein at a distance from the at least one working electrode;
- (b) a first signal generator coupled to the least one working electrode;
- (c) a second signal generator coupled to the counter electrode; and
- (d) a mixer adapted to receive a first signal reflected from the first signal generator, to receive a second signal from the first signal generator, and to mix the received first signal and the received second signal;

(e) a detector adapted to receive ~~receiving a~~ the signal mix ~~of a signal~~ ~~reflected from the first signal generator and a signal from the first signal generator, the detector~~ and to detect ~~detecting~~ modulation in the signal mix, thereby indicating hybridization in a sample in the fluid sample cell.

15. (Original) The system of Claim 14, wherein the first signal generator provides a signal of at least 1 MHz.

16. (Original) The system of Claim 14, wherein the at least one working electrode comprises an electrode surface covered in gold.

17. (Original) The system of claim 16, wherein the electrode surface has an area of at least 0.01 mm<sup>2</sup>.

18. (Original) The system of claim 14, wherein the at least one working electrode comprises an electrode surface covered with a self-assembled monolayer.

19. (Original) The system of Claim 14, wherein the first signal generator is coupled to the at least one working electrode by a directional coupler.

20. (Currently amended) The system of Claim 19, further comprising a ~~high-pass filter-bias Tee~~ connected between the directional ~~couple~~ coupler and the at least one working electrode.